

**Amendment and Response**

Page 2 of 7

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2003

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

**Remarks**

The Office Action mailed March 30, 2006 has been received and reviewed. The pending claims are claims 1-74. Reconsideration and withdrawal of the rejections are respectfully requested.

**Information Disclosure Statement**

Applicants have not received an initialed copy of the 1449 forms submitted with the Information Disclosure Statement filed on January 22, 2004. In addition, the Examiner returned a copy of the 1449 form submitted with the Information Disclosure Statement filed on December 16, 2003, but did not initial the Foreign Patents on that form. A copy of the 1449 forms and a copy of the date stamped postcards are enclosed as Exhibit C for the Examiner's convenience. Pursuant to the provisions of M.P.E.P. §609, Applicants request that a copy of the 1449 forms, marked as being considered and initialed by the Examiner, be returned with the next Official Communication.

**The Art Rejections**

The Examiner rejected claims 1-74 under 35 U.S.C. §102(b) as being unpatentable by Hossainy et al. (U.S. Patent No. 6,153,252). This rejection is respectfully traversed.

The Examiner rejected claims 1-74 under 35 U.S.C. §102(b) as being unpatentable by Whitbourne et al. (U.S. Patent No. 6,110,483). This rejection is respectfully traversed.

The Examiner rejected claims 1-74 under 35 U.S.C. §103(a) as being unpatentable over Hossainy et al. (U.S. Patent No. 6,153,252). This rejection is respectfully traversed.

The Examiner rejected claims 1-74 under 35 U.S.C. §103(a) as being unpatentable over Whitbourne et al. (U.S. Patent No. 6,110,483). This rejection is respectfully traversed.

Hossainy et al. is directed to a method of coating to prevent bridging in a stent. They disclose using polymer barrier layers to control drug release. The barrier can include

**Amendment and Response**

Page 3 of 7

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2003

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

homopolymers, blends, or multilayers of polymers. Columns 4-6 provide very long laundry lists of polymers, including both stable polymers and biodegradable polymers. There is no specific disclosure of miscible polymer blends, and no specific disclosure of the correlation of miscible polymer blends with the delivery (release) of an active agent (e.g., drug). Actually, only one copolymer was used in all the working examples. No polymer blend was exemplified.

Whitbourne et al. is directed to providing lubricious coatings. They disclose using a stabilizing polymer with a hydrophilic polymer and/or bioactive agent. Although blends of polymers are disclosed, columns 5-6 provide very long laundry lists of polymers, including stabilizing and hydrophilic polymers. Although they mention drug release and exemplify drug release formulations, there is no release data and no specific disclosure of the correlation of miscible polymer blends with the delivery (release) of an active agent (e.g., drug). In fact, Whitbourne et al. state that time release of drug could be controlled through the interactions between drug and stabilizing polymers (see, e.g., column 3, lines 56-59). Furthermore, Whitbourne et al. suggest that a stabilizing polymer is preferred to be crosslinkable to trap the hydrophilic components (see, e.g., column 4, lines 63-65 and column 6, lines 46-58). These concepts are not relevant to polymer miscibility, which is related to the polymer-polymer interactions. Although Example 15 includes two hydrophilic polymers: PVP and an acrylic copolymer with hydroxyl groups, and a hydrophobic drug, no release data is presented. Furthermore, it is not believed that such a polymer pair can control the release of the hydrophobic drug.

Thus, neither Hossainy et al. nor Whitbourne et al. provide a specific disclosure of a miscible polymer blend including an active agent as recited in Applicants' claims.

Both Hossainy et al. and Whitbourne et al. disclose laundry lists of polymers that include, among others, those recited by Applicants' claims (e.g., columns 4-6 of Hossainy et al. and columns 5-6 of Whitbourne et al.). Many of the individually listed polymers are defining classes, and thus, broad genera of polymers. Also, where the term "blend" is used (e.g., column 7, line 28 of Hossainy et al.), a "miscible" blend is not the only interpretation. See, for example, Exhibit A (Lipatov et al., "Thermodynamics of Polymer Blends," *Polymer Thermodynamics Library, Vol. 1*, Lancaster, PA, 1997, 7 pgs.) which states that "Utracki"<sup>15</sup> considers all the

## Amendment and Response

Page 4 of 7

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2003

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

mixtures of polymers as blends that may be either miscible or immiscible." Exhibit B (Utracki, *Polymer Alloys and Blends, Thermodynamics and Rheology*, New York, NY, 1990, 6 pgs.) defines "polymer blend" as "a mixture of at least two polymers or copolymers," and "miscible polymer blend" as a "polymer blend homogenous down to the molecular level." Thus, simply disclosing one or more particular polymers in a laundry list of polymers and the "blends thereof" does not specifically teach a miscible polymer blend, particularly one with an active agent therein, as recited in Applicants' claims. That is, there is no specific disclosure that includes a combination of polymers that inherently forms a miscible blend AND can control the delivery of an active agent in a tunable manner, which is a goal of the active agent delivery systems of Applicants' invention.

Accordingly, it is respectfully submitted that neither Hossainy et al. nor Whitbourne et al. provide an appropriate §102 rejection. "[I]t is not uncommon that a 'species' may be patentable, that is, satisfy sections 101-103, notwithstanding a prior art 'genus' " (e.g., *In re Ornitz*, 376 F.2d 330, 336, 153 USPQ 453, 458 (CCPA, 1967). Furthermore, "a prior genus which does not explicitly disclose a species does not anticipate a later claim to that species" (e.g., *D. Chisum, Chisum on Patents, Volume 1, Release No. 94, §3.02[2][b]* page 3, line 9 to page 4, line 2).

Applicants respectfully submit that neither Hossainy et al. nor Whitbourne et al. specifically exemplify or provide an enabling disclosure of the presently claimed "species," i.e., an active agent delivery system that includes an active agent and a miscible polymer blend. It is well settled that prior art under 35 U.S.C. §102(b) must sufficiently describe the claimed invention to have placed the public in possession of it. Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his own knowledge to make the claimed invention. Accordingly, even if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it is not enabling.

To be legally operative as effective prior art, "a reference must . . . enable one skilled in the art to make the anticipating subject matter." *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1566, 37 U.S.P.Q.2d (BNA) 1618, 1624 (Fed. Cir. 1996), *subsequent*

## Amendment and Response

Page 5 of 7

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2003

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

*appeal*, 156 F.3d 1351, 48 U.S.P.Q.2d (BNA) 1351 (Fed. Cir.), *reh'g, en banc, denied*, 1998 U.S. App. LEXIS 30846 (Fed. Cir. 1998) (citing *Chester v. Miller*, 906 F.2d 1574, 1576 n. 2, 15 U.S.P.Q.2d (BNA) 1333, 1336 n.2 (Fed. Cir. 1990) and *In re Donohue*, 766 F.2d 531, 533, 226 U.S.P.Q. (BNA) 619, 621 (Fed. Cir., 1985)). The single reference must describe the claimed invention, including all claim limitations, with "sufficient clarity and detail to establish that the subject matter existed in the prior art and that such existence would be recognized by persons of ordinary skill in the field of the invention." *Crown Operations Int'l, Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1375, 62 U.S.P.Q.2d (BNA) 1917, 1921 (Fed. Cir. 2002), *reh'g denied*, 2002 U.S. App. LEXIS 13283 (Fed. Cir. 2002) (citing *In re Spada*, 911 F.2d 705, 708, 15 U.S.P.Q.2d (BNA) 1655, 1657 (Fed. Cir. 1990) ("the reference must describe the applicant's claimed invention sufficiently to have placed a person of ordinary skill in the field of the invention in possession of it"); and *Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675, 678, 7 U.S.P.Q.2d (BNA) 1315, 1317 (Fed. Cir. 1988)). Furthermore, "invalidity based on anticipation requires that the assertedly anticipating disclosure enabled the subject matter of the reference and thus of the patented invention without undue experimentation." *Elan Pharms.*, 346 F.3d at 1052.

Despite this lack of an enabling disclosure of the presently claimed species, i.e., an active agent delivery system that includes an active agent and a miscible polymer blend, the Examiner asserts the theory of inherency. Applicants earnestly disagree with the Examiner's use of this theory. For inherency to apply, the missing descriptive information must necessarily be present in one of the cited documents such that one of skill in the art would recognize such a disclosure. "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill'" (*In re Robertson*, 49 USPQ2d 1949 (Fed. Cir. 1999) quoting *Continental Can Co. v. Monsanto Co.*, 20 USPQ2d 1746 (Fed. Cir. 1991)). See also MPEP 2112.

At least because there is no specific disclosure that includes a combination of polymers that inherently forms a miscible blend AND can control the release of an active agent in an adjustable manner, there can be no recognition by one of skill in the art that Applicants' claimed invention is necessarily present. Inherency must be a necessary result, not merely a

**Amendment and Response**

Page 6 of 7

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2003

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

possible result. "Inherency . . . may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." (In re Robertson, 49 USPQ2d 1949 (Fed. Cir. 1999) quoting In re Oelrich, 212 USPQ 323 (Fed. Cir. 1981)). Furthermore, Applicants' claimed invention would be inherent only if there is at least a reasonable likelihood that one of skill in the art could have discovered or recognized it without specific guidance. That is, the subject matter relied upon must be disclosed in a manner to place it in possession of the public. (See, e.g., Akzo N.V. v. United States Int'l Trade Comm'n, 1 USPQ2d 1241 (Fed. Cir. 1986)). Clearly, this is not the situation with the documents cited by the Examiner. Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §102.

With respect to the obviousness rejections, "[t]he fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a prima facie case of obviousness. In re Baird, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994)" (e.g., M.P.E.P. § 2144.08). Applicants respectfully submit that neither Hossainy et al. nor Whitbourne et al. provide guidance for one of skill in the art to select, as a polymer blend for an active agent delivery system, a miscible polymer as recited in the present claims.

In evaluating lack of disclosure regarding an obviousness rejection, the Court of Customs and Patent Appeals stated that "[s]ilence in a reference is hardly a proper substitute for an adequate disclosure of facts from which a conclusion of obviousness may justifiably follow." (See In re Burt and Walter, 148 U.S.P.Q. 548, 553 (C.C.P.A. 1966)).

Applicants respectfully submit that the selection of the particular relationships between the polymers and the active agent such that controlled delivery occurs is not a matter of routine experimentation and optimization of the composition. Absent Applicants' disclosure of the various parameters and their relationships, one would not be guided to obtain the claimed invention. This is particularly true in view of the very general teachings of Hossainy et al., which do not even suggest the use of a miscible polymer blend as advantageous relative to other polymer blends.

**Amendment and Response**

Page 7 of 7

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2003

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

As such, Applicants respectfully submit that the present claims are not obvious over Hossainy et al. or Whitbourne et al. Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §103.

**Summary**

It is respectfully submitted that the pending claims 1-74 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted

By

Muetting, Raasch &amp; Gebhardt, P.A.

P.O. Box 581415

Minneapolis, MN 55458-1415

Phone: (612) 305-1220

Facsimile: (612) 305-1228

Customer Number 26813

June 28, 2006  
Date

By: Ann M. Muetting

Ann M. Muetting

Reg. No. 33,977

Direct Dial (612) 305-1217

**CERTIFICATE UNDER 37 CFR §1.8:**

The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 28th day of

June, 2006, at 2:48 pm (Central Time).

By: Deb Schurmann

Name: Deb Schurmann

**Exhibit A**

# **Thermodynamics of Polymer Blends**

---

**YURI S. LIPATOV  
ANATOLY E. NESTEROV**

**POLYMER THERMODYNAMICS LIBRARY, VOL. 1**

**HOW TO ORDER THIS BOOK**

BY PHONE: 800-233-9936 or 717-291-5608, 8am-5pm Eastern Time  
BY FAX: 717-296-4638

BY MAIL: Order Department  
Technomic Publishing Company, Inc.  
851 New Holland Avenue, Box 3535  
Lancaster, PA 17604, U.S.A.

BY CREDIT CARD: American Express, VISA, MasterCard  
BY WWW SITE: <http://www.techpub.com>

**PERMISSION TO PHOTOCOPY-POLICY STATEMENT**

Authorization to photocopy items for internal or personal use, or the internal or personal use of specific clients, is granted by Technomic Publishing Co., Inc. provided that the base fee of US \$2.00 per copy, plus US \$ .25 per page is paid directly to Copyright Clearance Center, 222 Rosewood Drive, Danvers, MA 01923, USA. For those organizations that have been granted a photocopy licence by CCC, a separate system of payment has been arranged. The fee code for users of the Transactional Reporting Service is 1550-5886/06 \$2.00 + \$ .25.

**POLYMER THERMODYNAMICS LIBRARY, VOL. 1**

# Thermodynamics of Polymer Blends

**YURI S. LIPATOV**

**ANATOLY E. NESTEROV**

*Academy of Sciences of Ukraine*



LANCASTER - PA 17603



**Polymer Thermodynamics Library—Volume 1**

a TECHNOMIC Publication

*Published in the Western Hemisphere by*  
 Technomic Publishing Company, Inc.  
 851 New Holland Avenue, Box 3535  
 Lancaster, Pennsylvania 17604 U.S.A.

*Disseminated in the Rest of the World by*  
 Technomic Publishing AG  
 Mültenstrasse 44  
 CH-4005 Basel, Switzerland

Copyright © 1997 by Chemtec Publishing

All rights reserved. No part of this publication may be reproduced, stored or transmitted in any form or by any means without written permission of copyright owner. No responsibility is assumed by the Author and the Publisher for any injury or/and damage to persons or properties as a matter of products liability, negligence, use, or operation of any methods, product ideas, or instructions published or suggested in this book.

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

Main entry under title:

Polymer Thermodynamics Library—Volume 1: Thermodynamics of Polymer Blends

A Technomic Publishing Company book

Bibliography: p.

Includes index: p. 443

Library of Congress Catalog Card No. 97-62285  
 ISBN No. 1-56576-624-9

This Technomic Publishing Company, Inc. edition is produced under license between  
 Technomic Publishing Company, Inc. and Chemtec Publishing.

**Table of Contents**

<b>Preface</b>	ix
<b>Basic Principles of Thermodynamics of Polymer Solutions</b>	1
1.1 The Main Thermodynamic Characteristics of Solution	1
1.2 Regular Solutions. Hildebrand-Scatchard Equation	2
1.3 Phase Equilibrium in Solutions. Binodals and Spinodals	4
1.4 The Flory-Huggins Theory	9
1.4.1 Entropy of Mixing	10
1.4.2 The Heat and Free Energy of Mixing	11
1.5 Dilute Solutions of Polymers	13
1.6 Phase Separation in Polymer Solutions	16
<b>References</b>	30
<b>Statistical Theories of Polymer Solutions</b>	33
2.1 The Theory by Prigogine-Patterson	34
2.2 The Role of Various Contributions of the Mixing Parameters	42
2.3 Effect of Solvent Chain Length on the Interaction Parameters	44
2.4 New Flory Theory	48
2.5 Modification of the New Flory Theory	55
2.6 New Huggins Theory	59
2.7 Sanchez-Lacombe Theory	65
2.7.1 Equation of State	65
2.7.2 Mixtures of Liquids	67
2.7.3 Free Energy and Chemical Potential	69
2.7.4 Functions of Mixing	70
2.7.5 Phase Stability and Spinodal	71
2.8 Some Experimental Results of Thermodynamic Properties of Polymer Solutions	73
<b>References</b>	77
<b>Thermodynamics of Polymer Mixing</b>	81
3.1 Binary Mixtures	81
3.1.1 Application of the Theory of Regular Solutions to Thermodynamics of Polymer Mixing	83
3.1.2 Application of New Statistical Theories for Describing Thermodynamic Properties of Polymer Mixtures	88
3.1.3 The Application of the New Huggins Theory	88
3.1.4 The Sanchez-Lacombe Theory	101
3.1.4.1 Chemical Potentials	102
3.1.4.2 The Stability of Phase and Spinodal	104
3.1.4.3 Criterion of Miscibility of Polymer-polymer Mixture	107
3.2 Experimental Data on Thermodynamic Properties of Binary Polymer Mixtures	110
3.2.1 Phase Behavior of Binary Polymer Mixtures	117

3.2.2	Concentration and Temperature Dependences of Parameters of Thermodynamic Interactions in the Mixtures of Oligomers and Polymer Homologues	128
3.2.3	Influence of Various Factors on the Miscibility	143
3.2.3.1	Deuteration and Tacidity of Polymers	143
3.2.3.2	Branching of Chains	144
3.2.3.3	Effect of Pressure	144
3.2.3.4	Asymmetry of the Length of Statistical Segment	148
3.2.4	Possible Errors in Estimating the Miscibility of Mixtures Obtained from Solutions in a Common Solvent	148
3.3	Miscibility of Polymers at the Interface with Solid	151
3.3.1	Phase Diagrams of Filled Polymer Mixtures	151
3.3.2	Phase Separation in Thin Films of Polymer Mixtures at the Interface with Solid	151
3.3.3	Thermodynamic Interaction Parameters in Filled Polymer Mixtures	155
3.3.4	On the Equilibrium and Non-equilibrium Compatibilization of Polymer Mixtures	161
3.4	Ternary Polymer Systems	167
3.4.1	Ternary Systems Polymer-polymer-solvent	169
3.4.2	Ternary Polymer-polymer-polymer Systems	169
3.5	Thermodynamics of Formation of Stable Dispersion in Binary Polymer Mixtures	185
	<i>References</i>	205
		210
4	Homopolymer-copolymer and Copolymer-copolymer Blends	227
4.1	Mean-field Binary Interaction Models	227
4.1.1	Miscibility Windows	227
4.2	Effect of the Sequence Distribution in Copolymer on the Phase Behavior of Homopolymer-copolymer Mixtures	230
4.3	The Dependence of the Phase Behavior of Copolymer Mixtures of Various Compositions on the Sequence Distribution	235
4.4	The Effect of the Sequence Distribution in Copolymer and Its Compatibilizing Effect in Mixture of Two Immiscible Polymers	239
4.4.1	Mixtures of Homopolymers with Homologue Series of Polymers of Another Chemical Nature	243
4.5	Ternary Mixtures	251
4.8	Modified Theories of the Equation-of-state	259
	<i>References</i>	264
		271
5	Mechanism and Kinetics of Phase Separation in Polymer Solutions and Blends	275
5.1	Nucleation and Growth	275
5.2	Spinodal Mechanism of Phase Separation	277
5.3	Application of the Theory of Spinodal Decomposition to Polymeric Systems	277
		402

Some Experimental Results on Kinetics of Phase Separation in Solutions and Mixtures of Polymers	289
Factors Influencing the Kinetics of Phase Separation	320
Tacidity	321
Effects of Addition of Diblock-copolymers	323
Spinodal Decomposition Near Solid Surface	328
Shear-Induced Phase Separation	329
Phase Separation Accompanying Reactions of Polymer Blend Formation	334
Spinodal Decomposition in IPNs	334
Nucleation and Growth During IPN Formation	340
Some Features of Microphase Structure of IPNs	351
<i>References</i>	356
Interface in Demixing Solutions and Polymer Mixtures	363
Vrij-Roeberson Theory	364
Kammer's Theory	371
The Theory by Helfand	374
The Theory by Nose	380
Sanchez-Lacombe Theory	381
Other Theories of Polymer-polymer Interface	391
Scaling Principle in Describing the Interface	397
Some Experimental Data on the Interfacial Properties of Polymer Blends	400
Interfacial Tension	400
The Interfacial Width and Interfacial Profiles	401
Surface Segregation in Polymer Mixtures	401
Surface Segregation Near the Interface with Solid	408
Segregation of Block-copolymers at the Interface	412
Between Homopolymers	428
<i>References</i>	435
Nomenclature	435
Index	443

BEST AVAILABLE COPY

## Preface

Polymer alloys and blends belong to one of the most dynamic sectors of the polymer industry. This explains the great interest in the studies of their physical and mechanical properties, their structure, and the processes of their formation and manufacture. Thermodynamics of polymer blends is based on the classical theories of polymer solutions developed by Flory, Huggins, Prigogine, Patterson, Sanchez, and others as well as on the theories of the phase equilibrium and phase separation in solids developed by Cahn, Prigogine, and other authors. There are many books and reviews on the subject of the thermodynamics of polymer solutions. After the fundamental works by Flory,<sup>1</sup> Huggins,<sup>2</sup> and Tompa,<sup>3</sup> the following publications have been dedicated mainly to the problems discussing excluded volume. Theoretical investigations regarding this subject, performed before 1970, were systematically summarized as the so-called two-parameter theory in the book by Yamakawa,<sup>4</sup> and compared with an extensive experimental data. This first stage of research was immediately followed by a new theoretical approach, namely, the renormalization group theory. These developments, achieved until recently, can be found in books by Freed<sup>5</sup> and des Cloizeaux and Jannink.<sup>6</sup> However, the recent experimental data point out to the deficiencies in the two-parameter theory. These data were summarized and discussed by Fujita.<sup>7</sup> There have been published also some reviews.<sup>8,10</sup> The new developments and the fundamental contribution to the theory of polymer solution come from de Gennes<sup>11</sup> discussed in his famous book *Scaling Concepts in Polymer Physics*.

However, if presently there exists a voluminous scientific literature dedicated to various aspects of the physics and chemistry of polymer blends, there are no many books dedicated to the thermodynamics of mixing and thermodynamic behavior of polymer mixtures. This subject was presented in such fundamental works as *Polymer Blends* edited by Paul,<sup>12</sup> books by Olabisi, Robeson, and Shaw,<sup>13</sup> Hansen and Spierling,<sup>14</sup> Utracki,<sup>15</sup> and some other authors.<sup>16,17</sup>

Thermodynamic behavior of polymer blends determines the compatibility of the components, their morphological features, rheological behavior, microphase structure, and in such a way the most important physical and mechanical characteristics of blends.

This book is dedicated to the detailed analysis of the thermodynamics of polymer-polymer systems. This book is not intended as an introduction in the field but the knowledge of the main principles of thermodynamics is assumed. We attempted to consider the modern

state of thermodynamics of mixing and phase separation and to discuss both theoretical and experimental aspects of the problem. Chapters 1 and 2 discuss thermodynamics of polymer solutions and the most important theories describing the processes of dissolution and phase separation. These chapters give the reader a fundamental understanding of the present state of knowledge on the thermodynamics of polymer blends. Analyzing the thermodynamic behavior of polymer blends, we pay a special attention to the processes of phase separation and to the formation of an interphase between coexisting phases. The thermodynamic properties of an interphase play a very important role in the mechanical behavior of the blends.<sup>18</sup> One may say that formation of the interphase distinguishes the properties of blends from properties of solution. After all, the rheological and mechanical properties of polymer blends are determined by the compatibility of the components and by the degree of microphase separation that implies the formation of an interphase.

Some words about terminology. Although the concept of "compatibility" is widely used in the literature, we prefer to follow the definition given by Olabisi, Robeson, and Shaw.<sup>19</sup> We cite: "compatibility has been used by many other investigators involving various studies of polymer-polymer blend behavior to describe good adhesion between the constituents, average of mechanical properties, etc. The term 'miscibility' has been chosen to describe polymer-polymer blends with behavior similar to that expected of a single-phase system. The term miscibility... does not imply ideal molecular mixing but suggests that the level of molecular mixing is adequate to yield macroscopic properties expected of a single-phase material."

Another term that should be defined is: polymer alloys and blends. Both alloys and blends are produced by mixing two polymers in various conditions. Utracki<sup>16</sup> considers all the mixtures as blends that may be either miscible or immiscible. Alloys are formed, after Utracki, only after some modification of immiscible blends which allows to improve the compatibility, i.e., alloy is the result of some compatibilization. This compatibilization does not imply that the system becomes miscible and is only connected with some improvement of interactions at the interface between the two phases of immiscible mixture (a typical example is compatibilization obtained by the introduction in the homopolymer blend of diblock-copolymers composed of blocks corresponding to two homopolymers).

We propose another terminology<sup>18,19</sup> based on the thermodynamic considerations and including the analysis of the phase diagrams of binary mixtures as the basis for differentiation.

It is known that the most common and convenient method of mixing two polymers is by melt blending, which is typical for metallic

alloys. Generally, alloys are macroscopically uniform substances obtained by fusion of two or more metals, nonmetals, and organic compounds. In general, alloys are not obtained by simple mechanical mixing of the components. By fusing, the components may form mixtures of various phases. The phase state of an alloy in equilibrium can be determined from the phase diagram. It is known also that, for linear polymers, the phase diagrams are of two types, with upper and lower critical solution temperatures (UCST and LCST). Taking the phase diagrams as a basis, we give the following definitions:

- Alloys of linear polymers are binary or multicomponent systems that, when mixed in the molten state, they are situated in the region of the phase diagram corresponding to the mutual miscibility of the components and to the formation of one-phase solution. This means that the system is thermodynamically stable (at equilibrium) in the molten state. By cooling the melt, a structure develops which depends on the thermodynamic state at a given temperature. If by cooling, the system with UCST enters the region of unstable states in the phase diagram (immiscibility or thermodynamic incompatibility arises), then the structure becomes the two-phase structure and it is determined by the conditions of phase separation.

The structure depends on the degree of phase separation and on the mechanism of phase separation (nucleation or spinodal decomposition). The ratio and composition of two phases is determined by the kinetics and mechanism of phase separation. For binary systems with UCST, the mixing of the alloy components should be conducted in the region above spinodal and for the systems with LCST - below spinodal, i.e., in the range of one-phase solution. For systems with LCST, one-phase structure is preserved by cooling, i.e., a miscible system is maintained.

Blends of linear polymers are such binary systems that, by mixing in the molten state, they are not miscible and do not form one-phase system (they are not thermodynamically miscible). The components forming a blend may also have UCST or LCST. For systems with UCST, the formation of blend proceeds at temperatures below the binodal and for systems with LCST above the binodal. The transition from two-phase to one-phase state for systems with LCST is practically impossible by lowering temperature because of the high viscosity of the melt and the slowness of the mutual dissolution process. Thus, the structures of blends are deter-

mined by the degree of dispersion of one or both components achieved during mixing in the melt.

In such a way, depending on the temperature range of mixing, relative to the position of the binodal or spinodal, the same polymer pair may form both alloys and blends. The realization of both possibilities depends on the relationship between the temperature of phase separation for a given composition of a mixture and the glass transition temperatures or melting points of both components. Because the formation of blends or alloys by fusing the components (mixing in the molten state) is always followed by temperature reduction, the definitions given above allow to distinguish between the structural features of polymer alloys and blends. The analysis made above allows to conclude that two-phase or multi-phase blends are typical of systems with UCST, whereas one-phase alloys for systems with LCST.

The principle feature of polymer alloy consists of the incomplete phase separation in the system. By cooling a melt of two polymers the thermodynamic incompatibility of two components arises which causes the incomplete phase separation of the system. This incompleteness of the phase separation causes the development of both the microphase separation regions of various composition and transition or interphase zone between coexisting microregions. The system with incomplete microphase separation is not in the state of thermodynamic equilibrium. A segregated structure develops in the bulk because of these processes with a complex of specific properties: appearance of the regions with different density, composition and mechanical properties, appearance of the internal interphase boundaries, etc.

The same definition may be applied to the reactive mixtures capable of the formation of interpenetrating polymer networks. The transition from the initially one-phase mixture of components to cured two-phase system is connected with the phase separation and the phase-separated system may be attributed to alloy.

However, in the present book, where we consider the thermodynamic behavior of the polymer-polymer systems and do not deal with the peculiarities of their structure in a solid state, we will use the words "blends" and "mixtures" as a general, equivalent, and habitual terms. In reality, when we mix or blend two polymer components we do not know beforehand their thermodynamic behavior.

It is worth noting that there are no either fully miscible or fully immiscible mixtures. All depends on the phase diagram of the system, i.e., on the composition and temperature. At the same time, we fully agree with the statement<sup>13</sup> that "the two-phase system must be defined and contrasted with miscible system to delineate the two

subjects and to establish the criteria." One of the aims of this book is the analysis of conditions of miscibility and immiscibility.

These authors understand that the field of thermodynamics of polymer blends is too extensive to be covered in one book. There are many questions that have not been considered or were considered only briefly. However, we hope that this volume will further stimulate interest in this branch of physical chemistry of polymers.

Authors had worked with full comprehension. Each of us thanks the other for the mutual support and encouragement. We wish also to express our sincere gratitude to Dr. G. Wypych who initiated this work and who waited patiently for its result.

Institute of Macromolecular Chemistry,  
National Academy of Sciences of Ukraine,  
Kyiv, June 1997

## REFERENCES

1. P. J. Flory, *Principles of Polymer Chemistry*, Cornell Univ. Press, Ithaca, N.Y., 1953.
2. M. L. Huggins, *Physical Chemistry of Polymers*, Interscience, N.Y., 1958.
3. H. Tompa, *Polymer Solutions*, Butterworth, London, 1956.
4. H. Yamakawa, *Modern Theory of Polymer Solutions*, Harper and Row, N.Y., 1971.
5. K. F. Freed, *Renormalization Group Theory of Macromolecules*, Wiley-Interscience, N.Y., 1987.
6. J. des Cloizeaux and G. Jannink, *Polymers in Solutions*, Oxford Univ. Press, Oxford, 1980.
7. H. Fujita, *Polymer Solutions*, Elsevier, Amsterdam, 1990.
8. T. Hashimoto, *Current Theories in Polymer Science*, R. M. Ottranovic, L. A. Utracki, and S. Inoue, Eds., Hanser, N.Y., v. 2, p. 197 (1987).
9. J. D. Genton, M. San Miguel, and P. S. Bahai, in *Phase Transitions and Critical Phenomena*, D. Domb and U. L. Ledwith, Eds., Academic Press, London, v. 8, p. 267 (1983).
10. T. M. Aminabhavi, R. H. Balundgi, and S. S. Joshi, *J. Sci. Ind. Res.*, 47, 376 (1988).
11. P. de Gennes, *Scaling Concept in Polymer Physics*, Cornell Univ. Press, Ithaca-London, 1979.
12. Polymer Blends, D. R. Paul and J. W. Marlow, Eds., Academic Press, N.Y., 1978.
13. O. Olabisi, L. Robeson, and M. Shaw, *Polymer-Polymer Miscibility*, Academic Press, N.Y.-London, 1979.
14. A. Manson and L. Sperling, *Polymer Blends and Composites*, Plenum Press, N.Y., 1976.
15. L. A. Utracki, *Polymer Alloys and Blends*, Hanser Publishers, Munich-Vienna-New York, 1989.
16. *Polymer Alloys-Properties and Application* (in Japanese), Society of Polymer Science Japan, Tokyo, 1981.
17. S. Akiyama, T. Inoue, and T. Nishi, *Polymer Blends* (in Japanese), CMC, Tokyo, 1981.
18. Y. S. Lapinov, *Polymer Reinforcement, ChemTech Publ.*, Toronto, 1995.
19. Y. S. Lapinov, *Int. J. Polymer Mater.*, 17, 91 (1992).

**Exhibit B**

**Leszek A. Utracki**

# **POLYMER ALLOYS AND BLENDS**

**Thermodynamics and Rheology**



**Hanser Publishers, Munich Vienna New York**

**Distributed in the United States of America by Oxford University Press, New York  
and in Canada by Oxford University Press, Canada**

**The Author:**

Dr. Leszek A. Utracki, Associate Director, National Research Council of Canada, Industrial Materials Research Institute, Boucherville, Quebec, Canada

**Distributed in USA by**

Oxford University Press  
200 Madison Avenue, New York, N.Y. 10016

**Distributed in Canada by**

Oxford University Press, Canada  
70 Wynford Drive, Don Mills, Ontario M3C 1J9

**Distributed in all other countries by**

Carl Hanser Verlag  
Kolbergerstr. 22  
D-8000 München 80

The use of general descriptive names, trademarks, etc. in this publication, even if the former are not especially identified, is not to be taken as a sign that such names, as understood by the Trade Marks and Merchandise Marks Act, may accordingly be used freely by anyone.

While the advice and information in this book are believed to be true and accurate at the date of going to press, neither the authors nor the editors nor the publisher can accept any legal responsibility for any errors or omissions that may be made. The publisher makes no warranty, express or implied, with respect to the material contained herein.

**CIP-Titelaufnahme der Deutschen Bibliothek**

Utracki, Leszek A.: Polymer alloys and blends : thermodynamics and rheology / Leszek A. Utracki. - Munich ; Vienna ; New York : Hanser, 1989  
ISBN 3-446-14200-2

ISBN 3-446-14200-2 Carl Hanser Verlag, Munich, Vienna, New York

ISBN 0-19-520796-3 Oxford University Press, New York

All rights reserved. No part of this book may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording or by any information storage and retrieval system, without permission from the publisher.

Copyright © Carl Hanser Verlag, Munich, Vienna, New York 1990

Printed in the Federal Republic of Germany by C. H. Beck'sche Buchdruckerei, Nördlingen

## Part 1

INTRODUCTION TO POLYMER ALLOYS  
AND BLENDS

---

1.1 Historical Outline of the Industrial Development of Polymer Alloys and Blends . . . . .	1
1.2 The Reasons for and the Methods of Blending . . . . .	13
1.3 Fundamental Principles for Development of Polymer Alloys and Blends . . . . .	20
1.4 How to Design a Polymer Blend . . . . .	25
1.5 Final Comments . . . . .	27

---

1.1 Historical Outline of the Industrial Development of Polymer  
Alloys and Blends

The contemporary reader of polymer blend literature may be under the impression that blending is a recent development. When asked to name the first polymer blend an audience usually casts about 70% of its votes for "Noryl", 25% for ABS, with the remaining 5% for various blends listed in Table 1.2 later in the text.

This lack of historical perspective on the commercial development of polymer alloys and blends, PAB, is due to their rapid growth in importance during the 1980's. For example, in 1987, it was estimated that 60 to 70% of polyolefins and 23% of other polymers were sold as blends (but not necessarily identified as such). Furthermore, while during the late 80's the annual growth rate (AGR), of the plastics industry was 2 to 4%, that of PAB was 9 to 11% while the AGR of engineering blends was 13 to 17%. Clearly, the plastics industry is moving toward more complex systems. Whereas the use of polymers in composites and filled plastics is nearly 29%, the use of unmodified neat resin has shrunk to less than 50%. The future will bring a further increase of complexity in the form of multicomponent/multifunctional blends, foamed and reinforced PAB with more emphasis on enhanced optimization of material performance through processing.

## 1.1.1 Definitions

In the context of this volume the following terminology will be used:

- (i) *polymer*, polymeric material or resin with linear, branched or crosslinked structure whose degree of polymerization exceeds 50 to 70.
- (ii) *copolymer*, polymeric material synthesized from more than a single monomer.
- (iii) *engineering polymer (EP)*, a processable polymeric material, capable of being formed to precise and stable dimensions, exhibiting high performance at the continuous use temperature above 100°C, and having tensile strength in excess of 40 MPa.
- (iv) *polymer blend (PB)*, a mixture of at least two polymers or copolymers.



## 1 Introduction to Polymer Alloys and Blends

- (v) *homologous polymer blend (HPB)*, a mixture of two homologous polymers, usually narrow molecular weight distribution fractions of the same polymer.
- (vi) *miscible polymer blend (MPB)*, polymer blend homogenous down to the molecular level, associated with the negative value of the free energy of mixing:  
 $\Delta G_m \approx \Delta H_m \leq 0$ .
- (vii) *immiscible polymer blend*, any PB whose  $\Delta G_m = \Delta H_m > 0$ .
- (viii) *compatible polymer blend*, a utilitarian term indicating a commercially attractive polymer mixture, normally homogenous to the eye, frequently with enhanced physical properties over the constituent polymers.
- (ix) *polymer alloy (PA)*, an immiscible PB having a modified interface and/or morphology.
- (x) *compatibilization*, a process of modification of interfacial properties of an immiscible polymer blend, leading to the creation of a polymer alloy.
- (xi) *engineering polymer blend (EPB)*, a PB or PA either containing or having properties of the EP.

It is clear that the miscibility of PB, being defined in terms of the equilibrium thermodynamics, must be considered only within the range of independent variables (temperature, pressure, molecular weight, chain structure, etc.) under which the free energy of mixing is negative. Note that observed miscibility of a given polymer pair is insufficient for generalization of such behavior to other pairs of the same polymers or to another set of physical conditions.

As will be discussed in Part 2, the condition for  $\Delta G_m < 0$  can exist only if the binary polymer-polymer interaction coefficient,  $\chi_{12}$ , is negative. There are three contributions to  $\chi_{12}$ : dispersion forces, free volume and the specific interactions. Their relative magnitude and the temperature dependence is shown schematically in Fig. 1.1. In the Figure the dependency on the left is most frequently observed in low molecular weight solutions, while that on the right in polymer blends. The UCST and LCST indicate the upper and the lower critical solution temperature respectively. For  $UCST < T < LCST$  the mixture is miscible, i.e. for PAB the miscibility vanishes on heating above the LCST. In consequence, blending PB above LCST leads to a state of miscibility in the finished product which depends on the kinetics of phase separation during the post-processing cooling stage.

The rate at which the thermodynamic equilibrium can be achieved depends on the driving thermodynamic force, i.e. the polymer-polymer interaction coefficient, and the resisting rheological forces, i.e. the diffusivity. For example, it can be calculated that for polyolefin blends, where the interaction coefficient  $\chi_{12} \rightarrow 0$ , the time for thermodynamic equilibrium, depends on the low self diffusion coefficient. As a result the polyolefin blends prepared in a common solvent may show miscibility, whereas those prepared by mechanical mixing apparent immiscibility. Only detailed studies of the tendency of these blends to mix or to separate over a long period of time can answer the question of their true thermodynamic miscibility. However, miscible or not, most polyolefin blends are compatible, with an enhancement of their physical performance responsible for the predominance of blending in the polyethylene industry.

Another term which needs further explanation is polymer alloy (PA). The general relation between blends and alloys is shown in Fig. 1.2. PA constitutes a specific sub-class of PB. Virtually all high performance engineering blends are alloys. For practical reason PA can be subdivided into two categories: (A) those in which the compatibilization leads to very fine (usually sub-micron) dispersion so the molded part will show neither streaking nor excessive weld-line weakening, and (B) those where some compatibilizer is added in order to facilitate the formation of the desired morphology in a subsequent processing step. Most PA's belong to category A (e.g. BASF Ultranyl polyphenyleneether/polyamide blend). DuPont Sclar-PA polyamide/ ionomer blend (to be added to polyolefin and then blow molded) can serve as an example of category B. The methods of detecting polymer-polymer miscibility are

alogous polymers, usually  
polymer.  
is down to the molecular  
of mixing;

mercially attractive poly-  
enhanced physical proper-

rface and/or morphology.  
operties of an immiscible

ng or having properties of

he equilibrium thermody-  
t variables (temperature,  
e free energy of mixing is  
nsufficient for generaliza-  
o another set of physical

n exist only if the binary  
are three contributions to  
Their relative magnitude  
: 1.1. In the Figure the  
ar weight solutions, while  
: the upper and the lower  
T the mixture is miscible,  
In consequence, blending  
act which depends on the  
ge.

chieved depends on the  
tion coefficient, and the  
an be calculated that for  
time for thermodynamic  
sult the polyolefin blends  
e prepared by mechanical  
icity of these blends to mix  
n of their true thermody-  
ls are compatible, with an  
dominance of blending in

y (PA). The general rela-  
a specific sub-class of PB.  
ractical reason PA can be  
ization leads to very fine  
er streaking nor excessive  
dded in order to facilitate  
g step. Most PA's belong  
ic blend). DuPont Selar-  
1 blow molded) can serve  
r-polymer miscibility are

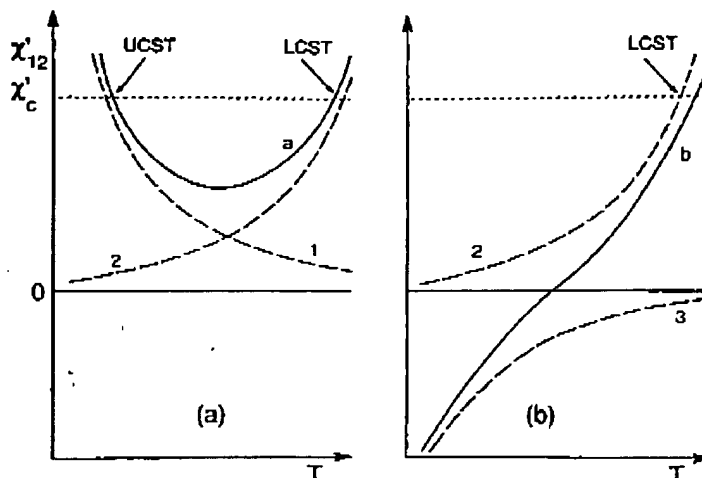


Fig. 1.1 Schematic representation of the temperature variation of the interaction parameter,  $\chi'_{12}$  (solid line) and its components: 1. dispersion forces, 2. free volume, and 3. specific interactions. The resulting graph (a) represents interactions encountered mostly in solutions with upper and lower solution temperatures, UCST and LCST respectively, whereas graph (b) is more typical of polymer blends where only LCST is visible. (Panerson and Robard, 1978).

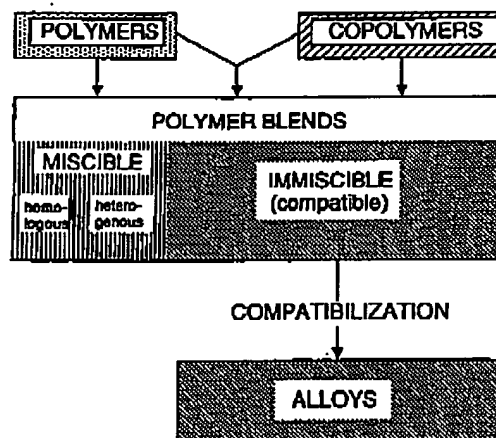


Fig. 1.2 Interrelations in polymer blend nomenclature.

## 4 1 Introduction to Polymer Alloys and Blends

discussed in Part 2.6. In most cases, since these do not allow for direct determination of either phase diagram,  $\Delta G_m$ ,  $\Delta H_m$  or  $\chi_{12}$ , they can only be taken as measures of apparent miscibility. The most popular of these is a plot of the compositional dependency of the glass transition temperature,  $T_g$ . The presence of two  $T_g$ 's is taken as an indication of immiscibility. In fact, detection of a single concentration dependent  $T_g$  only signifies that the size of the blend domains is below 15 nm. In Fig. 1.3 low frequency storage modulus is plotted as a function of temperature. The broken lines represent the behavior of neat polymers, the solid of 50:50 blend. The sudden drop of a modulus is associated with onset of molecular thermal motions in the region of  $T_g$ . The four schematics illustrate: 1. miscible, 2. immiscible, 3. partially miscible, and 4 immiscible blend with fine dispersion and broad glass transition region.

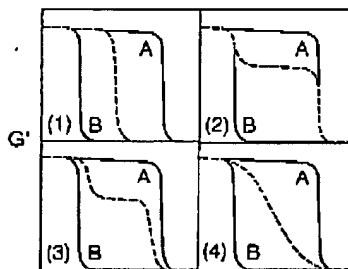


Fig. 1.3 Schematic representation of temperature dependence of storage shear modulus for polymer A, polymer B (solid lines) and their 50:50 mixture (broken line). Case (1) A and B are miscible, Case (2) A and B are immiscible, Case (3) The miscibility is limited to low concentration of A in B and B in A, Case (4) Blend with fine dispersion (compatibilized).

## 1.1.2 Development of Commercial Alloys and Blends

In Table 1.1 the dates of commercialization of major thermoplastics are listed. The table is intended to highlight main steps in development of plastics industry. The interested readers will find more exhaustive information in monographs on the subject (*Winding and Hlat*, 1961; *Mason*, 1972; *Schwartz and Goodman*, 1982; *Seymour*, 1982; *Morawetz*, 1985). Table 1.2 provides a more complete listing of commercial polymer blends. Blending of rubbers predates that of thermoplastics by nearly a century. The original idea of gaining extra performance by blending must be credited to Thomas Hancock, who by mixing natural rubber with gutta percha obtained a mixture which was easily applied for waterproofing cloth.

Polyvinylchloride has been known in laboratories since 1872 but became commercial only in 1927 after the advantage of plasticization was discovered. However, development of acrylonitrile rubber (NBR), and in 1942 the discovery of its ability to permanently plasticize PVC spurred rapid penetration of the market. The PVC/NBR blend was the first commercial thermoplastics blend in the modern sense of the word. In the same year, 1942, Dow Chemical Co. introduced Styralloy-22 (a precursor of interpenetrating polymer network materials, IPN), of polystyrene and polybutadiene. Thus the term "alloy" for the first time was used in reference to a polymeric mixture. In 1942 development of mechanical mixtures of NBR with poly(styrene-co-acrylonitrile), SAN, (known as ABS type A) was an important step in starting a flood of polymer alloys and blends. As one may note in the lists of

**EXHIBIT C**

<b>INFORMATION DISCLOSURE STATEMENT</b>	<b>Atty. Docket No.:</b> P-10998.00 (M&R 134.01930101)	<b>Serial No.:</b> 10/640,853
	<b>Applicant(s):</b> Sparer et al.	<b>Confirmation No.:</b> 9178
	<b>Application Filing Date:</b> Aug. 13, 2003	<b>Group:</b> 3763
	<b>Information Disclosure Statement mailed:</b> JANUARY 22, 2004	

**U.S. PATENT DOCUMENTS**

Examiner Initial	Copy Enclosed	Document Number	Date	Name	Class	Subclass	Filing Date If Appropriate
		5,676,972	10/14/97	Galiatsatos et al.			
		5,900,246	05/04/99	Lambert			
		6,074,660	06/13/00	Jamiolkowski et al.			
		6,077,916	06/20/00	Laurencin et al.			
		6,224,894 B1	05/01/01	Jamiolkowski et al.			
		2001/0032014 A1	10/18/01	Yang et al.			
		2002/0018795 A1	02/14/02	Whitbourne et al.			

**FOREIGN PATENT DOCUMENTS**

Examiner Initial	Copy Enclosed	Document Number	Date	Country	Class	Subclass	Translation	
							Yes	No
	X	EP 0 281 482 A1	09/07/88	Europe				
	X	EP 0 347 145 A2 & A3	12/20/89	Europe				
	X	EP 0 592 870 A1	04/20/94	Europe				
	X	EP 1 023 879 A2 & A3	08/02/00	Europe				
	X	EP 1 110 561 A2 & A3	06/27/01	Europe				
	X	WO 89/03860 A1	05/05/89	PCT				
	X	WO 93/00058 A1	01/07/93	PCT				
	X	WO 96/23601 A1	08/08/96	PCT				
	X	WO 99/47127 A1	09/23/99	PCT				
	X	WO 01/78626 A1	10/25/01	PCT				
	X	WO 02/13883 A2 & A3	02/21/02	PCT				

**EXAMINER****Date Considered**

\*Examiner: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

OMB No. 0651-0011

Page 2 of 2

<b>INFORMATION DISCLOSURE STATEMENT</b>	Atty. Docket No.: P-10998.00 (M&R 134.01930101)	Serial No.: 10/640,853
	Applicant(s): Sparer et al.	Confirmation No.: 9178
	Application Filing Date: Aug. 13, 2003	Group: 3763
	Information Disclosure Statement mailed: JANUARY <u>22</u> , 2004	

	X	WO 02/26281 A1	04/04/02	PCT				
	X	WO 02/058756 A2 & A3	08/01/02	PCT				
	X	WO 03/018083 A2 & A3	03/06/03	PCT				
	X	WO 03/022323 A1	03/20/03	PCT				

**OTHER DOCUMENTS (Including Authors, Title, Date, Pertinent Papers, etc.)**

Examiner Initial	Copy Enclosed	Document Description
	X	Anonymous, "Endoluminal Stent with Releasable Radioisotope," <i>Research Disclosure Journal, Kenneth Mason Publications, Hampshire, GB, 447(101)</i> .
	X	Apicella et al., "Poly(ethylene oxide) (PEO) and Different Molecular Weight PEO Blends Monolithic Devices for Drug Release," <i>Biomaterials.</i> , 1993;14(2): 83-90.
	X	Kwok et al., "Design of Infection-Resistant Antibiotic-Releasing Polymers: I. Fabrication and Formulation," <i>J. Control Release.</i> , 1999 Dec 6;62(3):289-299.
	X	Nishi et al., "Newly Developed Stent Graft with Micropored and Heparin Impregnated SPU Film: Long-Term Follow-Up Study In Vivo," <i>Interventional Neuroradiology, Italy</i> , 2001;7:161-166.

<b>EXAMINER</b>	<b>Date Considered</b>
<small>*Examiner: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</small>	

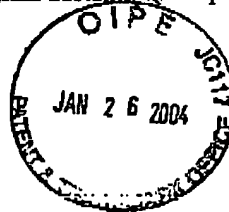
**RECEIVED  
CENTRAL FAX CENTER****JUN 28 2006**

Receipt is hereby acknowledged for the following in the U.S. Patent and Trademark Office:

Applicant(s): Sparer et al.  
Serial No.: 10/640,853      Confirmation No.: 91-78  
Filed: August 13, 2003  
Title: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL  
DEVICES, AND METHODS

Enclosed: Information Disclosure Statement (2 pgs); copy of International  
Search Report for PCT/US03/25368 (2 pgs); 1449 forms (2 pgs); copies of 19  
documents cited on the 1449 forms; and transmittal document (in triplicate).


Mailed: JANUARY 22 2004  
Docket: P-10998.00 (M&R 134.01930101)



AMM/pah

OMB No. 0651-0011

Page 1 of 2

<b>INFORMATION DISCLOSURE STATEMENT</b> 	Atty. Docket No.: P-10998.00 (M&R 134.01930101)	Serial N. : 10/640,853
	Applicant(s): Sparer et al.	Confirmation No.: 9178
	Application Filing Date: Aug. 13, 2003	Group: 3763
	Information Disclosure Statement mailed: <b>DECEMBER 16, 2003</b>	

## U.S. PATENT DOCUMENTS

Examiner Initial	Copy Enclosed	Document Number	Date	Name	Class	Subclass	Filing Date If Appropriate
QR		4,100,309	07/11/78	Micklus et al.			
		4,873,308	10/10/89	Coury et al.			
		4,876,126	10/24/89	Takemura et al.			
		5,059,166	10/22/91	Fischell et al.			
		5,069,899	12/03/91	Whitbourne et al.			
		5,525,348	06/11/96	Whitbourne et al.			
		5,722,984	03/03/98	Fischell et al.			
		5,837,313	11/17/98	Ding et al.			
		5,871,437	02/16/99	Alt			
		5,997,517	12/07/99	Whitbourne			
		5,986,034	11/16/99	DiDomenico et al.			
		6,086,547	07/11/00	Hanssen et al.			
		6,110,483	08/29/00	Whitbourne et al.			
		6,111,052	08/29/00	DiDomenico et al.			
		6,149,678	11/21/00	DiDomenico et al.			
QR		6,306,176	10/23/01	Whitbourne			

## FOREIGN PATENT DOCUMENTS

Examiner Initial	Copy Enclosed	Document Number	Date	Country	Class	Subclass	Translation	
							Yes	No
	X	EP 0 832 644 B1	04/01/98	Europe (with English language title and claims)				X
	X	EP 0 993 308 A2	12/30/98	Europe (equivalent to WO 98/58680)				X
	X	WO 92/11877 A1	07/23/92	PCT				

<b>EXAMINER</b> 	<b>Date Considered</b> 3/24/2006
<small>*Examiner: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</small>	

**RECEIVED  
CENTRAL FAX CENTER****JUN 28 2006**

Receipt is hereby acknowledged for the following in the U.S. Patent and Trademark Office:

Applicant(s): Sparer et al.  
Serial No.: 10/640,853 Confirmation No.: 9178  
Filed: August 13, 2003  
Title: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL  
DEVICES, AND METHODS

Enclosed: Preliminary Amendment (17 ~~pgs~~); Information Disclosure  
Statement (3 pgs); copies of 5 applications; 1449 forms (2 pgs); copies of 11  
documents cited on the 1449 forms; and transmittal document (in triplicate).

Mailed: DECEMBER 16, 2003  
Docket: P-10998.00 (M&R 134.01930101)



AMM/pah



**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

**BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☒ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**